Scientific Abstract

The age-adjusted prevalence of peripheral arterial disease (PAD) in the U.S. population has been estimated to approach 12% [1]. The clinical consequences of occlusive peripheral arterial disease (PAD) include pain on walking (claudication), pain at rest, and loss of tissue integrity in the distal limbs; the latter may ultimately lead to amputation of a portion of the lower extremity. Surgical bypass techniques and percutaneous catheter-based interventions may be used to successfully revascularize the limbs of certain patients with PAD. In many patients, however, the anatomic extent and distribution of arterial occlusion is too severe to permit relief of pain and/or healing of ischemic ulcers. No effective medical therapy is available for the treatment of such patients.

The purpose of this clinical protocol is to investigate the efficacy and safety of therapeutic angiogenesis achieved in this case by percutaneous catheter-based delivery of the gene encoding vascular endothelial growth factor (VEGF) in patients with PAD. The rationale for this human protocol is based upon preclinical studies performed in a rabbit model of hindlimb ischemia. These studies are described in detail below and in the manuscripts enclosed in the Appendix to this proposal. In brief, a single intra-arterial bolus of VEGF recombinant human protein, delivered percutaneously to the ischemic limb via an intravascular catheter, resulted in angiographic, hemodynamic, physiologic, and histologic evidence of augmented collateral artery development. Subsequently, similar results were achieved using an angioplasty catheter with a hydrogel-coated balloon to deliver 400 μg of a plasmid containing the cDNA for VEGF to the internal iliac artery in the same animal model.

Accordingly, we propose to employ arterial gene (VEGF) therapy to treat rest pain and/or ischemic leg ulcers in 12 patients considered not to be candidates for conventional revascularization techniques.